REMARKS

Claims 1-13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Yasukawa et al. *J. Biol. Chem.*, **270:** 25328-25331 (1995) ("Yasukawa") in view of LaVallie et al. *Bio/Technology* **11:** 187-193 (1993) ("LaVallie"). Specifically, the Examiner states:

> "[Yasukawa] teach the transformation of *E. coli* with separate plasmids for the production of soluble foreign proteins. One plasmid encodes the foreign protein, and the second plasmid encodes the *E. coli* thioredoxin gene. The co-expression of the foreign protein with the thioredoxin protein in the host cell results in a large increase of soluble foreign produced, versus host cells which express only the foreign protein without thioredoxin. See Figure 2, for example. In the Discussion, [Yasukawa] refer to [LaVallie] as citation number (27) and note that their system is superior to that of [LaVallie] in that the thioredoxin protein is not expressed as a fusion protein with the foreign protein. ..... [LaVallie] is cited to note that both the thioredoxin and the foreign protein can be expressed from the same plasmid and not necessarily from separate plasmids."
>
> "..... The difference between what applicant claims and the teachings of [Yasukawa] is that [Yasukawa] teach the co-transformation of separate plasmids into *E. coli* for the separate production of the thioredoxin and the heterologous protein within the host cell, while the applicant teaches the co-expression of these proteins from genes found separately on the same plasmid. Absent evidence to the contrary, the co-expression of separate genes on the same plasmid would have been obvious given the combined teachings of the prior art."

Applicants believe that the prior art cited by the Examiner does not render obvious the pending claims of the instant application. Nevertheless, Applicants submit herewith a Declaration Under 37 C.F.R. § 1.131 signed by Paula D. Ravnikar and Robert Greenberg establishing that the claimed invention was reduced practice prior to the effective date of Yasukawa, thus obviating the Examiner's rejection. Specifically, the 131 Declaration demonstrates that applicants had expressed in bacteria, prior to October 1, 1995, a heterologous protein in soluble form using a single plasmid

construct containing both the *E. coli* thioredoxin gene and a gene encoding a heterologous protein.

In response to the April 23, 1998 supplemental letter regarding compliance with the Sequence Rules, applicants have enclosed a substitute computer readable form (CRF), a substitute paper copy of the "Sequence Listing" and have amended the specification to incorporate the substitute "Sequence Listing". In addition, applicants have enclosed a statement that the content of the substitute CRF and the substitute paper copy are the same and do not include new matter.

Applicants believe that the above remarks and the attached Declaration adequately address all of the outstanding issues, and that all claims under consideration are in condition for allowance. Should that not be the case, and should any unresolved issues remain, Applicants hereby request that the Examiner contact the undersigned attorney at (908) 298-5061.

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE U.S. POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON D.C. 20231 ON

August 14, 1998

DATE OF DEPOSIT

Immac J. Thampoe

REGISTERED REPRESENTATIVE

8/14/98

SIGNATURE AND DATE OF SIGNATURE

Respectfully submitted,

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